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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/111,123	07/06/1998	HABIB ZAGHOUANI	8114-005-WO-CIP	5474

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CATALYST LAW GROUP, APC
9710 SCRANTON ROAD, SUITE S-170
SAN DIEGO, CA 92121

EXAMINER	
SZPERKA, MICHAEL EDWARD	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 01/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/111,123	ZAGHOUANI, HABIB	
	Examiner	Art Unit	
	Michael Szperka	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-7 and 21-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-7, and 21-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on November 4, 2005 has been entered.

Applicant's amendment and response received November 4, 2005 is acknowledged.

Claims 1, 4, 21, and 23 have been amended.

Claims 8-20 have been canceled.

Claims 1, 3-7, and 21-27 are pending and under examination in this office action.

Specification

2. Applicant is thanked for the amendments to the specification to correct minor typographical corrections such as misspelled words.

Claim Objections

3. Applicant's amendments to the claims received November 4, 2005 have overcome the objection of record.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. The rejection of claims 1, 3-7 and 21-27 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement has been withdrawn due to applicant's amendments to the claims received November 4, 2005. Specifically, the claims now recite that the T cell receptor agonist is specific for autoreactive T cells associated with a recited autoimmune disease

6. The rejection of claims 1, 4, 21 and 23 under 35 U.S.C. 112, first paragraph, for lack of enablement has been withdrawn due to applicant's amendments of the claims received November 4, 2005 that specify the relationship between the antagonists and the autoimmune disorders being treated.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

8. Claims 1, 3-4, and 21-24 stand rejected under 35 U.S.C. 102(e) as being anticipated by Deo et al., (U.S. Patent Number 5,837,243, of record, see entire document) for the reasons of record set forth in the office actions mailed August 10, 2004 and June 3, 2005 and as evidenced by Ukkonen et al. (J. Exp. Med, 1986, 163:952-971, see entire document) and as evidenced by Kuby (Immunology, 1992, W.H. Freeman and company, pages 208-211, see entire selection).

Applicant's arguments filed November 4, 2005 have been fully considered but they are not persuasive. Applicant has amended the claims to recite a mechanism by which the claimed fusion proteins are thought to work, and has repeated the argument that this mechanism, which is now recited in the claims, is different from that taught in the prior art and hence the rejection should be withdrawn.

The examiner respectfully disagrees for the reasons of record. First, the fusion protein taught by Deo et al. meets the structural requirements of the fusion protein recited in the instant claims, and as such any function that results from said structure would be inherent.

Second, the examiner believes that applicant is incorrect in the statement that the fusion construct of Deo et al. work by a different mechanism from that of the instant claimed products. Applicant argues that the constructs of Deo et al. work through a competitive mechanism that disrupts the interaction between MHC and TCR. This does not appear to be correct, since Deo et al clearly teach that their fusion proteins effectively increase the delivery of peptides to APCs *in vivo* and that that the antigenic epitopes present in the fusion protein can be effectively processed and presented on MHC class II molecules (see entire document, particularly example 7, most particularly lines 25-37 of column 27, lines 21-24 of column 32, and lines 12-35 of column 32). Applicant's apparent confusion concerning this competition mechanism appears to arise from the experiments disclosed in lines 12-35 of column 32 wherein Deo et al. sought to determine if their model peptide antagonist worked as an antagonist because it preferentially binds to MHC class II molecules as compared to an agonist peptide, or if the model peptide antagonist works as an antagonist due to the interactions of the antagonist peptide/MHC class II complex with a TCR. Deo et al. determined that the antagonism was the result of interactions between the TCR and the complex comprising the antagonist peptide in the peptide binding grove of an MHC class II molecule and was not due to differences in the ability of peptides to bind to MHC class II molecules (see particularly lines 12-14 of column 32). Applicant's further comments concerning the timing of peptide association with MHC class II molecules, and how these differ between the teachings of Deo et al. and applicant are confusing. It was well known in the art that material internalized via Fc receptor mediated endocytosis is delivered to

lysosomes, and that MHC class II molecules are loaded with peptides such acidic vesicles (Ukkonen et al., J. Exp. Med., 1986, 163:952-971, see entire document, particularly the title, and Kuby, J. Immunology, 1992, W.H. Freeman and Company, pages 208-211, see particularly Figure 9-16). The statements and teachings of Deo et al. are not in variance with the teachings of the art concerning the association of peptides with MHC class II molecules. As such, the fusion proteins taught by Deo et al. are internalized by binding to an FcR on an APC, are degraded in an intracellular compartment such that an antagonist peptide epitope within the fusion protein can associate with an MHC class II molecule, and then this complex of MHC class II/antagonist peptide is then transported to the cell surface to interact with the TCR of an autoreactive T cell, exactly the same way as applicant's fusion protein is taught as working.

As such the rejection is maintained.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office Action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 1, 5, 21 and 25 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Deo et al., (U.S. Patent Number 5,837,243, of record, see entire document) in view of Karin et al. (J. Exp. Med, 1994, 180: 2227-2237,of record, see entire document) for the reasons of record set forth the office actions mailed August 10, 2004 and June 3, 2005

Applicant's arguments filed November 4, 2005 have been fully considered but they are not persuasive. Applicant has argued that since the fusion protein taught in Deo et al. works by a different mechanism that the fusion protein of the instant invention, and since this deficiency is not remedied by the teachings of Karin et al., the rejection should be withdrawn. As explained above, applicant's statements concerning mechanistic differences between the fusion proteins are incorrect, and the rejection is hereby maintained.

11. Claims 1, 6, 21 and 26 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Deo et al., (U.S. Patent Number 5,837,243,of record, see entire document) in view of Kuchroo et al., (J. Immunol. 1994, 153: 3326-3336, of record, see entire document) for the reasons of record set forth in the office actions mailed August 10, 2004 and June 3, 2005.

Applicant's arguments filed November 4, 2005 have been fully considered but they are not persuasive. Applicant has argued that since the fusion protein taught in Deo et al. works by a different mechanism that the fusion protein of the instant invention, and since this deficiency is not remedied by the teachings of Kuchroo et al.,

the rejection should be withdrawn. As explained above, applicant's statements concerning mechanistic differences between the fusion proteins are incorrect, and the rejection is hereby maintained.

12. Claims 1, 7, 21 and 27 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Deo et al., U.S. Patent Number 5,837,243 in view of Elliott et al. (J. Clin. Invest., 1996, 98: 1602-1612), Kuchroo et al., (J. Immunol. 1994, 153: 3326-3336) and Karin et al. (J. Exp. Med, 1994, 180: 2227-2237) for the reasons of record set forth the office actions mailed August 10, 2004 and June 3, 2005.

Applicant's arguments filed November 4, 2005 have been fully considered but they are not persuasive. Applicant has argued that since the fusion protein taught in Deo et al. works by a different mechanism that the fusion protein of the instant invention, and since this deficiency is not remedied by the teachings of Elliott et al. and /or Karin et al. and/or Kuchroo et al., the rejection should be withdrawn. As explained above, applicant's statements concerning mechanistic differences between the fusion proteins are incorrect, and the rejection is hereby maintained.

Double Patenting

13. Claims 1, 3-4, 6, 21-24 and 26 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-16 of U.S. Patent No. 6,737,057. Although the conflicting claims are not identical, they are

not patentably distinct from each other for the reasons or record set forth in the office actions mailed August 10, 2004 and repeated June 3, 2005.

Applicant's arguments filed November 4, 2005 have been fully considered but they are not persuasive. Applicant argues that the instant claims are more specific than the patented claims and thus the patented claims cannot anticipate the instant claims. Patented claims recite that the antagonist peptides to be used come from MBP and PLP, known autoantigens in multiple sclerosis, and as such the fusion constructs of the patented claims would specifically target autoreactive T cell in MS. The instant claims are actually broader in scope in that they recite three different autoimmune diseases (rheumatoid arthritis, type I diabetes mellitus, and MS), and constructs comprising MBP or PLP would not be effective against rheumatoid arthritis or type I diabetes. As such the rejection is maintained.

14. No claims are allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Szperka whose telephone number is 571-272-2934. The examiner can normally be reached on M-F 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michael Szperka, Ph.D.
Patent Examiner
Technology Center 1600
January 6, 2006

Patrick J. Nolan, Ph.D.
Primary Examiner
Technology Center 1600